Adherence Concepts for the Cancer Patient

Benyam Muluneh, PharmD, BCOP, CPP

Objectives

• Discuss the shift from intravenous to oral chemotherapy over the past few decades
• Assess the various dimensions of adherence
• Manage patients who are non-adherent to oral chemotherapy
• Explain how to advocate for legislation that can improve access to oral chemotherapy
Adherence: Not so straightforward

“Adherence is the *single most important* modifiable factor that *compromises* treatment outcome.”

- World Health Organization, 2003
Pros and Cons

Benefits
- Convenient
- Patient Empowerment
- Decreased toxicity
- Increased efficacy

Concerns
- Adherence
- Cost
- Storage/handling
- Therapy monitoring

Adherence to Therapy

**Definition:** Extent to which a patient’s behavior coincides with medical advice

**Consequences of Non-adherence**

- Poor outcomes
- Increased Toxicity
- Increased health care costs

Non-adherence in chronic diseases

**Frequency of Administration**

Per Day
- Once → 80%
- Twice → 70%
- Three times → 65%
- Four times → 50%

$100 Billion per year in health-care costs

Higher in acute vs. chronic diseases

43-78% in clinical trials

Non-adherence in cancer: Major barrier to positive outcomes

Percent Adherence Over Six Cycles of Capecitabine in Adjuvant Breast Cancer
CALGB 60104

Consequences

Non-adherence literature

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Diagnosis</th>
<th>OA</th>
<th>Method</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demissie et al. / 2001</td>
<td>Breast Cancer</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>15% d/c</td>
</tr>
<tr>
<td>Partridge et al. / 2003</td>
<td>Breast Cancer</td>
<td>Tamoxifen</td>
<td>Refill data</td>
<td>13% not filling rx</td>
</tr>
<tr>
<td>Atkins et al. / 2006</td>
<td>Breast Cancer</td>
<td>Tamoxifen</td>
<td>Self-report</td>
<td>55% non-adherent</td>
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<tr>
<td>Barron et al. / 2007</td>
<td>Breast Cancer</td>
<td>Tamoxifen</td>
<td>Refill data</td>
<td>22% non-persistence</td>
</tr>
<tr>
<td>Darkow et al. / 2007</td>
<td>CML</td>
<td>Imatinib</td>
<td>Refill data</td>
<td>31% interruption</td>
</tr>
<tr>
<td>Guth et al. / 2008</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>Self-report</td>
<td>11% non-adherent</td>
</tr>
<tr>
<td>Owusu et al. / 2008</td>
<td>Breast Cancer</td>
<td>Tamoxifen</td>
<td>Refill data</td>
<td>49% d/c</td>
</tr>
<tr>
<td>Kimmick et al. / 2009</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>Refill data</td>
<td>36% not filling rx</td>
</tr>
<tr>
<td>Noens et al. / 2009</td>
<td>CML</td>
<td>Imatinib</td>
<td>BAAS¹</td>
<td>33% non-adherent</td>
</tr>
<tr>
<td>Hersman et al. / 2010</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>Refill data</td>
<td>32% d/c</td>
</tr>
<tr>
<td>Patridge et al. / 2010</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>MEMS²</td>
<td>25% non-adherent</td>
</tr>
<tr>
<td>Marin et al. / 2010</td>
<td>CML</td>
<td>Imatinib</td>
<td>MEMS²</td>
<td>26% non-adherent</td>
</tr>
<tr>
<td>Eliasson et al. / 2010</td>
<td>CML</td>
<td>Imatinib</td>
<td>MEMS²</td>
<td>20% non-adherent</td>
</tr>
<tr>
<td>Nekhljudov et al. / 2011</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>Refill data</td>
<td>21% d/c</td>
</tr>
<tr>
<td>Neugut et al. / 2011</td>
<td>Breast Cancer</td>
<td>Endocrine</td>
<td>Refill data</td>
<td>21% non-persistence</td>
</tr>
<tr>
<td>Streeter et al. / 2011</td>
<td>Various</td>
<td>Various</td>
<td>Refill data</td>
<td>10% abandonment</td>
</tr>
<tr>
<td>Bhatia et al. / 2012</td>
<td>ALL</td>
<td>6-MP</td>
<td>MEMS²</td>
<td>10% non-adherent</td>
</tr>
</tbody>
</table>
CLOSER LOOK

UNDERSTANDING THE DIMENSIONS OF ADHERENCE

Dimensions of Adherence

- Health system
- Social/economic
- Condition-related
- Therapy-related
- Patient-related

Health System

- Poorly developed health services
  - Poor medication distribution systems
  - Lack of knowledge and training of health care providers
  - Lack of incentives on feedback and performance

Social / Economic

- Poor socioeconomic status
- Poverty
- Illiteracy
- Low level of education
- Unemployment
- Lack of effective social support networks
- Unstable living conditions
- Long distance from treatment center
- High cost of transport
- High cost of medication,
- Changing environmental situations, culture and lay beliefs about illness and treatment, and family dysfunction
**Condition**

- Severity of symptoms
- Level of disability
  - Physical
  - Psychological
  - Social
  - Vocational
- Rate of progression and severity of the disease
- Availability of effective treatments

**Therapy**

- Complexity of the medical regimen
- Duration of treatment
- Previous treatment failures
- Frequent changes in treatment
- Immediacy of beneficial effects
- Side-effects and the viability of medical support to deal with them
Our experience

- **Objective**: to document and analyze patient perceptions as they relate to adherence of their oral antineoplastics
- **Additional objectives of this study were**:  
  - To determine where patients obtain information about their medications  
  - To address patient perceptions of drug-food interactions by assessing patient understanding of administration instructions related to taking their medication with or without food
Inclusion Criteria

- Adults (≥18 years old)
- English-speaking
- Diagnosis of CML, mRCC, breast cancer, GI malignancies
- Oncology care from UNC Hospitals and Clinics
- Single oral antineoplastic therapy

CML = chronic myeloid leukemia
mRCC = metastatic renal cell carcinoma

Survey Development

- Validated adherence survey
- Questions based on Likert scale
  - [Always, frequently, sometimes, never]
- Areas of focus
  - Frequency and reasons for reducing/skipping doses
  - Sources of information for oral antineoplastic (OA) use
  - Perceived importance of food-drug effects
  - Ease of understanding directions on vial label

Chew et al Fam Med 2004;36(8):588-94
Patients

152 total patients identified (28=BC, 62=CML, 40=RCC, 22=GI)

17 Excluded
(3=non-English speakers, 3=hospice, 4=deceased, 3=no longer on therapy, 3=mentally ill, 1=pediatric patient)

40 did not have a clinic appointment during study period

95 patients approached

93 patients completed survey (BC=22, CML=33, RCC=29, GI=8)

2 patients refused

98% response rate

Demographic Information

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of therapy (≤6 months)</td>
<td>51%</td>
</tr>
<tr>
<td>Gender (Female)</td>
<td>51.1%</td>
</tr>
<tr>
<td>Age group (&gt;50 years old)</td>
<td>58.7%</td>
</tr>
<tr>
<td>Education (Some College)</td>
<td>68.1%</td>
</tr>
</tbody>
</table>

Length of Diagnosis

- <1 year: 1%
- 1-3 years: 23%
- 4-5 years: 25%
- >5 years: 37%
- Don't Know: 14%
Notable Findings

- Don’t always think about last time they ate: 44%
- Incorrect food-drug administration: 14%
- Sometimes forget their OA: 30%
- Sometimes cut back their OA: 21%
- Don’t tell their MD they cut back their OA: 38%

UNC’s Adherence study:
Barriers to appropriate use of oral chemotherapy

- Confusion or misunderstanding about the timing of drug with food
- Forgetfulness in oral antineoplastic administration
- Reducing/stopping drug without informing MD
- Difficulty understanding directions on the drug vial label
STRATEGIES FOR MANAGEMENT

COMPREHENSIVE CARE

Cycle of Therapy

MD Visit

Patient

Therapy Selection

Adherence Tips

Access to Care

Transitions of Care
**ASSESSING ADHERENCE - Morisky Medication Adherence Scale**

**DO YOU TAKE YOUR MEDICATIONS THE RIGHT WAY?**

- Do you ever forget to take your prescription drugs?  
  - Yes (0) No (1)
- Are you careless at times about taking your drugs?  
  - Yes (0) No (1)
- Do you sometimes stop taking your drugs when you feel better?  
  - Yes (0) No (1)
- Do you sometimes stop taking your drugs if they make you feel worse?  
  - Yes (0) No (1)

**Score Interpretation**

- ≥8 Suggests adherence
- <8 Suggests non-adherence

**Assessing Adherence – CML Data**

<table>
<thead>
<tr>
<th>Medication Adherence Questionnaire</th>
<th>Score</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you forget to take your medication(s) this morning?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Have you run out of medication since your last visit?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Do you ever take your medication(s) later than your usual time?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>If you feel worse when taking your medication(s), do you stop taking it?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Do you think that you take too many medications?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Do you ever forget to take your medication(s)?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Do you know the name(s) of your medication(s)?</td>
<td>Yes (1) No (0)</td>
<td></td>
</tr>
<tr>
<td>Do you ever miss doses of your medication(s)?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Does a change in your daily routine modify the way you take your medication(s)?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
<tr>
<td>Do you sometimes skip doses of your medication(s) when you feel better?</td>
<td>Yes (0) No (1)</td>
<td></td>
</tr>
</tbody>
</table>

ASSESSING ADHERENCE – ONE QUESTION

Since the last time we saw you, about how many doses of your _____ do you think you may have missed?

Assessing Adherence

Administer Medication Adherence Questionnaire

Was the score ≥8?

Patient is likely adherent to TKI therapy.

Was the score <8 OR do you suspect nonadherence?

Contact pharmacy and calculate Medication Possession Ratio (MPR)
Medication Possession Ratio (MPR)

- Obtain records of at least 2 consecutive medication refills.
- Enter data (fill dates, days supply) into the Excel spreadsheet.

- In the above example, the MPR is 0.9375, or 93.75%.

Helpful hints

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgetfulness</td>
<td>Alarm Clock</td>
</tr>
<tr>
<td></td>
<td>Family Members</td>
</tr>
<tr>
<td>Side Effects</td>
<td>Close Follow-up</td>
</tr>
<tr>
<td></td>
<td>Early Management</td>
</tr>
<tr>
<td>Questions</td>
<td>Empowerment</td>
</tr>
<tr>
<td>Cost</td>
<td>Medication Assistance</td>
</tr>
<tr>
<td>Complex Regimen</td>
<td>Written Care Plan*</td>
</tr>
</tbody>
</table>

*Example: www.medactionplan.com
Patient calendars

<table>
<thead>
<tr>
<th>Date</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sun 20</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 1 tab</td>
</tr>
<tr>
<td>Mon 21</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 2 tabs</td>
</tr>
<tr>
<td>Tue 22</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 1 tab</td>
</tr>
<tr>
<td>Wed 23</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 2 tabs</td>
</tr>
<tr>
<td>Thu 24</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 1 tab</td>
</tr>
<tr>
<td>Fri 25</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 2 tabs</td>
</tr>
<tr>
<td>Sat 26</td>
<td>Panatinib 15 mg, Dexamethasone 1.5 tabs in the morning and 1.5 tabs in the afternoon, Mercaptopurine 1 tab</td>
</tr>
</tbody>
</table>

Take mercaptopurine at least 1 hour after evening meals. Avoid milk and citrus products.

ELECTRONIC ADHERENCE MONITORING PROGRAMS

<table>
<thead>
<tr>
<th>App</th>
<th>Engagement</th>
<th>Functionality</th>
<th>Aesthetics</th>
<th>Information</th>
<th>Subjective quality</th>
<th>MARSb total score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medisafe</td>
<td>0.94</td>
<td>0.90</td>
<td>0.93</td>
<td>0.83</td>
<td>1.00</td>
<td>0.92</td>
</tr>
<tr>
<td>MedicineList</td>
<td>0.74</td>
<td>0.90</td>
<td>0.87</td>
<td>0.93</td>
<td>0.78</td>
<td>0.84</td>
</tr>
<tr>
<td>CareZone</td>
<td>0.78</td>
<td>0.90</td>
<td>0.93</td>
<td>0.84</td>
<td>0.70</td>
<td>0.83</td>
</tr>
<tr>
<td>My PillBox</td>
<td>0.76</td>
<td>0.83</td>
<td>0.77</td>
<td>0.68</td>
<td>0.53</td>
<td>0.71</td>
</tr>
<tr>
<td>Desescat</td>
<td>0.56</td>
<td>0.90</td>
<td>0.80</td>
<td>0.80</td>
<td>0.55</td>
<td>0.70</td>
</tr>
<tr>
<td>MyMeds</td>
<td>0.52</td>
<td>0.75</td>
<td>0.87</td>
<td>0.55</td>
<td>0.48</td>
<td>0.63</td>
</tr>
<tr>
<td>My heart, my life</td>
<td>0.60</td>
<td>1.00</td>
<td>0.83</td>
<td>0.82</td>
<td>0.58</td>
<td>0.77</td>
</tr>
<tr>
<td>MyMedManager</td>
<td>0.50</td>
<td>0.83</td>
<td>0.70</td>
<td>0.63</td>
<td>0.33</td>
<td>0.60</td>
</tr>
<tr>
<td>Pill Reminder (Aplicativos Legans)</td>
<td>0.36</td>
<td>0.80</td>
<td>0.60</td>
<td>0.33</td>
<td>0.25</td>
<td>0.47</td>
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<tr>
<td>Medisafe</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

MD Visit

- Patients should always voice their preferences
- They should NOT walk away feeling like a question was not answered or information wasn’t clear
- Patients should be encouraged to write-down questions and answers

Patient education: Key Questions

- Why do I need this drug?
- How long will I stay on it?
- What are the risks of this drug?
- How have other patients like me responded?
- What are alternatives to this therapy?
Patient Education

- Written care plan
- Adverse effects
  - Management and tracking systems
- Food-drug administration education techniques

<table>
<thead>
<tr>
<th>Morning</th>
<th>Evening</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 am - Lapatinib (Tykerb)</td>
<td>8 pm - Dinner</td>
</tr>
<tr>
<td>8 am - Breakfast</td>
<td>8:30 pm - Capecitabine (Xeloda)</td>
</tr>
<tr>
<td>8:30 am - Capecitabine (Xeloda)</td>
<td></td>
</tr>
</tbody>
</table>

Therapy Selection

- Dosage adjustment
  - Organ dysfunction
  - Adverse Effects
- Simplified treatment regimen
  - In accordance to patient’s health care literacy
- Supportive care
  - Fatigue, N/V, diarrhea, neuropathy, rash
Access to care

• Proactively verify insurance coverage

• Specialty pharmacy services
  – Let your physician know if you use a specialty pharmacy or mail order

• Timely delivery of drug

• Track of time to refill

Access to Care

• If insurance denies coverage, there are other options available:
  – Manufacturer assistance
  – Grants from service organizations (e.g.: Leukemia Legislation Society, American Cancer Society)
  – If prescriptions filled at UNC Hospitals, resources available to further simplify process

• Legislation
  – Oral Chemotherapy Parity
IMPROVING ACCESS

PARITY LAWS

Chemotherapy payment process

Insurance Plan

Medical

Pharmacy

IV Chemotherapy

Outpatient Services

Oral Chemotherapy

Specialty Tier
Prescription Abandonment

- Patient and Plan Characteristics Affecting Abandonment of Oral Oncolytic Prescriptions by Streeter et al.

N=10,508 patients with Medicare and commercial insurance for whom oral anti-cancer therapy was initiated between 2007 and 2009

10% of cancer patients failed to fill their initial prescriptions for oral oncolytics

Claims with cost-sharing over $500 were four times more likely to be abandoned than claims with cost-sharing of $100 or less (25% vs. 6%)

Medicare coverage and lower income were also related to higher rates of abandonment.

16% of newly initiated oral oncolytics required an out-of-pocket cost of greater than $500

45.5% of Medicare patients face cost sharing greater than $500 for their first oral oncolytic prescription

The disparity

<table>
<thead>
<tr>
<th>Blue Cross Blue Shield Plan B Coverage*</th>
<th>Pharmacy Plan (out-pocket: $2,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Plan (out-of-pocket-max: $3,000)</td>
<td></td>
</tr>
<tr>
<td>IV Chemotherapy ($7,300)</td>
<td></td>
</tr>
<tr>
<td>Outpatient Infusion Services ($4,000)</td>
<td></td>
</tr>
<tr>
<td>Imaging Tests (PET, CT, MRI, etc.) ($2,000)</td>
<td></td>
</tr>
<tr>
<td>Doctor’s Visit ($200)</td>
<td></td>
</tr>
<tr>
<td>Physical Therapy ($250)</td>
<td></td>
</tr>
<tr>
<td>Surgical Procedure ($20,000)</td>
<td></td>
</tr>
<tr>
<td>Radiation Services ($10,000)</td>
<td>Oral Chemotherapy ($8,000 per month)</td>
</tr>
<tr>
<td>Laboratory Tests ($500)</td>
<td></td>
</tr>
<tr>
<td>Hospitalization ($2,500 per day)</td>
<td></td>
</tr>
</tbody>
</table>

*BCBNC 2013 Blue Advantage Plan B for an Individual
Avalere Health analysis of NAMCP member data
Oral chemotherapy parity legislation

42 states have enacted oral chemotherapy access laws:
2008 Oregon
2009 Indiana, Iowa, Hawaii, District of Columbia
2010 Vermont, Connecticut, Kansas, Colorado, Minnesota
2011 Illinois, New Mexico, Texas, New York, Washington
2012 New Jersey, Virginia, Maryland, Nebraska, Delaware, Louisiana
2013 Massachusetts, Oklahoma, Utah, Nevada, Florida, Rhode Island, California
2014 Maine, Missouri, Wisconsin, Kentucky, Georgia, Arizona, Ohio
2015 Wyoming, South Dakota, West Virginia, Mississippi, North Dakota, New Hampshire
2016 Alaska, Pennsylvania

HR 1801: Cancer Drug Coverage Parity Act of 2013

113th CONGRESS
1st SESSION
H. R. 1801

To amend the Employee Retirement Income Security Act of 1974, the Public Health Service Act, and the Internal Revenue Code of 1986 to require group and individual health insurance coverage and group health plans to provide for coverage of oral anti-cancer drugs on terms no less favorable than the coverage provided for anticancer medications administered by a health care provider.

IN THE HOUSE OF REPRESENTATIVES
APRIL 26, 2013

Mr. HIGGINS (for himself, Mr. MOORE, Ms. TAYLOR of Maine, Mr. CULLEN, Mrs. CAPPO, Ms. GILMARTIN, Ms. WILSON of Florida, Mr. HARRIS of Texas, Mr. RINGO of New York, Mr. RANGER, Mr. JAMES of Washington, Mr. McGOVERN, Mr. Peters of California, Mr. WOLF, Mr. MORA, and Mr. FARR) introduced the following bill, which was referred to the Committee on Energy and Commerce, and in addition to the Committees on Ways and Means and Education and the Workforce, for a period to be subsequently determined by the Speaker, in each case for consideration of such provisions as fall within the jurisdiction of the committee concerned.
Conclusions

• Adherence is an important consideration for patients on oral chemotherapy
• There are a variety of dimensions that contribute to poor adherence
• A multi-pronged, systematic approach to medication adherence is necessary to achieve patient adherence
• Access to expensive oral chemotherapy is one major barrier which could be overcome by legislation such as parity laws

“Drugs don’t work in patients who don’t take them”
- C. Everett Koop, M.D.